Pharmacia & Upjohn

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Global Regulatory Affairs
Janine L. Holmes
Regulatory Manager
Promotion Review
0632-298-130
Telephone No. (616) 833-8548
Facsimile No. (616) 833-8237

July 22, 1998

Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Dr., Rm 1-23
Rockville, MD 20857

Dear Sir or Madam:

As a company engaged in the promotion of prescription drug products and devices, we appreciate the opportunity to comment on the 8 June 1998 Federal Register Notice that presents the proposed rule for dissemination of information on unapproved/new uses for marketed drugs, biologics, and devices (Docket No. 98N-0222).

As a general matter, Pharmacia & Upjohn (P&U) is concerned that FDA's proposed rule violates the intent of Section 401 of the FDA Modernization Act (FDAMA) by imposing significant new requirements and constraints to narrow Section 401. Section 401 was crafted to enable the dissemination of valuable information in a controlled manner. The proposed rule, by virtue of it's definitions and requirements, will nearly inhibit, rather than facilitate, the dissemination of scientific information on new uses in contrast to Congress' clear intent. We are aware that this general concern has been expressed by the Pharmaceutical Research and Manufacturers of America (PhRMA), and believe it is important to strongly support this position.

As a member company of PhRMA, P&U aligns itself with their objections to the proposed rule, specifically as they relate to the type of information that may be disseminated, and the various aspects concerning the submission and review process. Our specific comments and objections on the proposed rule are:

98N-0222

Pharmacia & Upjohn
7000 Portage Road
Kalamazoo, MI 49001-0199
USA

Telephone (616) 833-4000

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Subpart A

99.3(g): P&U objects to the definition of "new use" as it appears in the *preamble* to the proposed rule. FDA's proposed definition of "new use" in *99.3(g)* mirrors the statutory definition, but the expansive interpretation of this definition in the preamble would remove the right of a manufacturer to distribute certain information on approved uses of a drug that have been historically allowed. Specifically, references to patient subgroups and comparative claims have been historically allowed if consistent with the approved indication, and adequately supported by data. We align ourselves with PhRMA on this issue, and strongly object to FDA's attempt to bring within the new dissemination provisions promotional practices that were permitted prior to enactment of Section 401.

Subpart B

99.101(a): P&U is gravely concerned that the proposed rule, as written, will supersede previous related guidance. P&U refers FDA to its guidance appearing in the October 8, 1996, Federal Register entitled "Guidance to Industry on Dissemination of Reprints of Certain Published, Original Data." This guidance allows for the dissemination of reprints of articles reporting the results of the pivotal trials relied on by FDA in its approval of a drug, device, or biologic product. This dissemination is allowed even though such articles may contain effectiveness rates, data, analyses, uses, regimens, or other information that is different from the approved labeling. P&U objects to any language in the rule that results in the inability of industry to disseminate such articles per the previous guidance.

99.101(a)(2)(i): P&U objects to the provision that the reprint or article copy intended for dissemination must be published. We advocate acceptance of final manuscripts or pre-prints of articles that have cleared the peer-review process. We propose that the journal acceptance letter be included in any submission containing a pre-print.

99.101(b)(1): P&U objects to the virtual exclusion of reference texts from the category of information to be disseminated. It is our belief that this violates the intent of Section 401, which stipulates only that a reference publication "include information about a clinical investigation..." The proposed regulation requires not only that a reference publication be about a clinical investigation that is scientifically sound, but that the reference report the study in a "reasonably comprehensive" manner. It is our position that reference texts should be viewed under a different standard, and not be required to provide a comprehensive review of a study to qualify for dissemination.

P&U refers FDA to their guidance appearing in the October 8, 1996, Federal Register entitled "Guidance for Industry Funded Dissemination of Reference Texts." It is our position that the final rule be consistent with this guidance, and not supersede its instruction.

Additionally, under *(b)(1)* of this subpart, we object to the categorical exclusion of review articles (termed review abstracts here) from the definition of "scientifically sound." If an abstract or review article is about a clinical investigation, and would be considered to be scientifically sound by experts, it satisfies the criteria of Section 401 even though it does not present comprehensive details about the clinical investigation. Individual articles upon which the review or abstract is based may be provided to FDA for it's 60-day review, and subsequent determination of scientific soundness. As provided for elsewhere in the rule, FDA may require balancing statements or accompanying information as it deems necessary.

99.101(b)(2): P&U requests clarification of the statement: "Such reprint, copy of an article, or reference publication shall not be disseminated with any information that is promotional in nature." This statement, interpreted literally, could preclude a sponsor from delivering an approved promotional piece or message on a labeled use during the same office visit or detail. We request that the statement be revised to reflect the exclusion of "...any information that is promotional in nature and related to the new use."

Subpart C

99.201(c): P&U requests that FDA clarify that the appropriate Review Division will also be a recipient of the submission in addition to DDMAC etc.

99.201(d): P&U objects that there is no provision for the sponsor to be notified when a complete submission has been received and the 60-day clock starts. We request that FDA provide acknowledgment of the receipt of a submission, and set a time period (e.g., 15 working days) within which it will notify a company whether its submission is complete.

Subpart D

99.301(a): P&U requests that the language in this part be altered to read "Within 60 days after receiving a submission under this part, FDA *shall* (instead of *may).*

P&U requests that it be clarified/stated in this part that a sponsor may begin dissemination of material in the event that FDA has not responded within 60 days.

Additionally, we request that *99.301(a)* provide for an opportunity for a manufacturer to meet with FDA concerning determinations that it may not disseminate information, or that additional information is needed to determine compliance.

99.301(a)(4): P&U objects that there is no provision for dialogue between FDA and the manufacturer in the event that FDA requires a company to maintain records that will identify *individual* recipients of the information to be disseminated. FDA should provide notice and the opportunity to meet in this situation.

Subpart E

99.401: P&U aligns itself with PhRMA's position that a sponsor should be given opportunity and a clear mechanism for appealing any requirement for corrective action. In addition, P&U advocates that a manufacturer be permitted to continue to disseminate the information in question pending the outcome of any appeal proceedings, with the exception of those instances in which a significant safety issue or public health concern exists.

Subpart F

99.501(b): P&U objects to the provision for semiannual reports and summaries on the progress of ongoing clinical research relating to the safety or effectiveness of the new use. P&U does not observe a "semiannual" requirement for these updates in the statute, and believes these reporting requirements can be fulfilled through standard IND or NDA reporting requirements.

Again, we appreciate the opportunity to comment on this proposed rule. We look forward to issuance of the final rule, and resulting implementation of Section 401 of FDAMA.

Sincerely,
Pharmacia & Upjohn Company

Janine L. Holmes
Regulatory Manager
Global Regulatory Promotion & Labeling

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Janine Holmes 299-130 616-833-8548

TO

Dockets Management Branch (HFA-305)
Food and Drug Administration
12420 Parklawn Dr., Rm 1-23
Rockville MD 20857

Margaret M. Dotzel 301-827-5321

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